

(A)-N-acetyl-Cys;

where A is angiotensin I SEQ ID NO: 1.

Please add the following new claims 40-45:

40. (New) An immunogen as claimed in claim 39 comprising said angiotensin derivative coupled to m-maleimidobenzoyl-N-hydroxysulphosuccinimide ester.

41. (New) An immunogen as claimed in claim 39 wherein said angiotensin derivative is N-acetyl-Cys-(A).

B2  
42. (New) An immunogen as claimed in claim 39 wherein said angiotensin derivative is Tyr-(A) SEQ ID NO: 7.

43. (New) An immunogen as claimed in claim 39 wherein said angiotensin derivative is N-acetyl-Cys-Gly-(A).

44. (New) An immunogen as claimed in claim 39 wherein said angiotensin derivative is Cys-(A) SEQ ID NO: 8.

#### REMARKS

Claims 1-39 are pending in the application, of which claims 1-38 have been withdrawn from consideration as being drawn to a non-elected invention. By the foregoing amendments, claims 40-44 have been added so that the claims under consideration now consist of claims 39-44. No new matter has been introduced.

Support for the amended claim 39 and the new claims 40-44 can be found throughout the specification and claims as filed. In particular, support for the additional subject matter in claim

39 can be found in originally filed claim 13. The m-maleimidobenzoyl-N-hydroxysulphosuccinimide ester of claim 40 can be found on page 14 of the specification and in Example 2 and is particularly useful as it allows the immunogen construct to be prepared using aqueous chemistry, thus obviating the need for removal of a non-aqueous solvent. Finally, support for new claims 41-44 can be found in originally filed claim 29 and correspond to the sub-species listed therein.

#### ***Sequence Listing***

Enclosed with this response is a sequence listing in paper and computer readable form in accordance with the requirements of 37 CFR §§ 1.821-1.825. The submission contains no new matter. The information recorded in computer readable form is identical to the written sequence listing.

#### ***Information Disclosure Statement***

Applicant notes that references 5 and 6 were submitted as received from the International Searching Authority. Applicant is trying to locate corresponding English language patent documents and/or obtain a translation so that these references may be considered by the Examiner.

#### ***Claim Rejection - 35 USC 102(b)***

Claim 39 has been rejected under 35 U.S.C. §102(b) as being anticipated by the article by Peeters et al. (reference no. 7 cited by applicant on the Information Disclosure Statement). This rejection is respectfully traversed and is believed to be obviated in view of the foregoing amendments and the following remarks.

The Examiner has asserted that Peeters et al. teaches a polypeptide immunogen capable of when conjugated to a carrier of inducing antibodies in an immunized subject that recognize epitopes of Angiotensin I and concluded that this anticipates the present invention.

This rejection is obviated in view of the foregoing amendments, and the amended claims are clearly novel and unobvious over Peeters et al.

Furthermore, Peeters et al. is directed to simply demonstrating that certain coupling reagents can be used to produce immunogenic conjugates. This in no way relates to or suggests the claimed compounds of the present invention which can be used to produce conjugates useful in immunotherapy or prophylaxis. Applicants had unexpectedly and surprisingly found that angiotensin I could successfully be used as a hapten in an immunoconjugate for direct or indirect use in therapy or prophylaxis of diseases associated with the renin-angiotensin system (RAS). This finding was unexpected and surprising in view of the teachings of the prior art that angiotensin I is very rapidly degraded to angiotensin II in vivo. Accordingly, applicants' use of angiotensin I rather than the short-chain and longer-lived angiotensin II as a hapten was directly counter to the teachings of the prior art. Furthermore, applicants discovered that not only is angiotensin I effective, but it is superior to angiotensin II, as clearly demonstrated by the experiments set forth in the specification. See for example Table 3 on pages 32-33 of the specification.

Additionally, since angiotensin I gave a different result from angiotensin II, it is quite evident that the angiotensin I immunoconjugates are not simply bioprecursors of the "equivalent" angiotensin II amino conjugates.

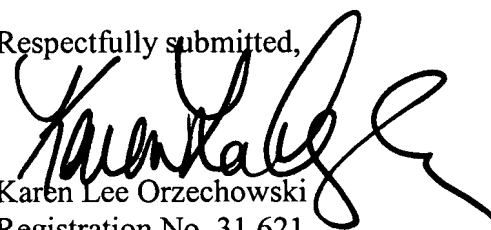
Accordingly, this rejection is believed to be inapplicable to the presently claimed invention and reconsideration and withdrawal of the same is respectfully requested.

It is not believed that extensions of time or fees are required, beyond those, which may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions

Response and Amendment  
Application No. 09/470,997  
Filing Date: December 23, 1999  
Page 5 of 7

are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims or the additional of independent claims in excess of three) is hereby authorized to be charged to Deposit Account No. 50-0548 and the undersigned is requested to be notified of any such charges.

Respectfully submitted,



Karen Lee Orzechowski  
Registration No. 31,621

Date: January 16, 2002

LINIAK, BERENATO, LONGACRE & WHITE  
6550 Rock Spring Drive, Suite 240  
Bethesda, MD 20817  
Telephone: (301) 896-0600  
Facsimile: (301) 896-0607

**CERTIFICATION OF FACSIMILE TRANSMISSION**

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office at Fax No. \_\_\_\_\_ on the date shown below.

Karen Lee Orzechowski

Signature

Date

**CERTIFICATE OF MAILING**

I hereby certify that this correspondence and any attachments thereto are being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, DC 20231, on January 16, 2002.

Karen Lee Orzechowski

Via Courier

## APPENDIX - MARKED UP AMENDMENTS

### In the claims:

39. (Amended) A polypeptide immunogen capable when conjugated to a carrier of inducing antibodies in an [immunised] immunized subject, [that recognize] which antibodies recognize epitopes of angiotensin I, angiotensin II and/or angiotensinogen, said immunogen comprising an angiotensin derivative selected from the group consisting of:

(A)-Gly-Cys SEQ ID NO: 3;

(A)-Cys SEQ ID NO: 5;

(A)-Tyr SEQ ID NO: 6;

N-acetyl-Cys-(A);

Tyr-(A) SEQ ID NO: 7;

N-acetyl-Cys-Gly-(A);

Cys-(A) SEQ ID NO: 8; and

(A)-N-acetyl-Cys;

where A is angiotensin I SEQ ID NO: 1.

40. (New) An immunogen as claimed in claim 39 comprising said angiotensin derivative coupled to m-maleimidobenzoyl-N-hydroxysulphosuccinimide ester.

41. (New) An immunogen as claimed in claim 39 wherein said angiotensin derivative is N-acetyl-Cys-(A).

42. (New) An immunogen as claimed in claim 39 wherein said angiotensin derivative is Tyr-(A) SEQ ID NO: 7.

Response and Amendment  
Application No. 09/470,997  
Filing Date: December 23, 1999  
Page 7 of 7

---

43. (New) An immunogen as claimed in claim 39 wherein said angiotensin derivative is N-acetyl-Cys-Gly-(A).

44. (New) An immunogen as claimed in claim 39 wherein said angiotensin derivative is Cys-(A) SEQ ID NO: 8.